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The convergent validity of the Scale for the Evaluation and Identification of Seizures, Epilepsy and Anticonvulsant Side Effects-B (SEIZES-B)

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THE CONVERGENT VALIDITY OF THE SCALE FOR THE EVAUALTION AND IDENTIFICATION OF SEIZURES, EPILPESY AND ANTICONVULSANT SIDE EFFECTS-B (SEIZES-B)

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ABSTRACT

Prevalence rates of epilepsy in individuals with intellectual disability (ID) are much higher than in the general population. Although antiepileptic drug (AED) therapy is considered the first line of treatment, a significant number of individuals on AEDs still do not achieve total seizure control. Further, many individuals experience side effects (SE) from long-term AED use. The assessment of AED SE in individuals with ID and epilepsy is an important aspect of treatment. The present study focused on the Scale for the Evaluation and Identification of Seizures, Epilepsy, and Anticonvulsant Side Effects-B (SEIZES-B), developed to assess SE from AED use in adults with ID and epilepsy. The purpose of this study was two-fold. First, the psychometric properties of the SEIZES-B were investigated. Interrater reliability of direct observations was explored using a licensed epileptologist and registered nurse as informants. Interrater reliability between observers was poor. The SEIZES-B was then compared to the epileptologists' direct observation rating to provide an estimate of convergent validity. Correlational analyses were low and non-significant. Second, 45 participants were compared across three groups (those with epilepsy taking AEDs, those with a diagnosis of epilepsy not taking AEDs, and those without epilepsy taking antipsychotic medications) on SE profiles of the SEIZES-B. Significant differences were not found across the groups. Results and implications of these data are discussed.

INTRODCTION

Individuals with epilepsy and intellectual disabilities (ID) often experience side effects (SE) from antiepileptic drug (AED) use. Despite the availability of newer AEDs associated with less severe SE, individuals with ID remain susceptible (Ettinger, Barr, & Solomon, 2001). Traditional standards for assessing SE in the general population often rely on self-report. Individuals with ID, however, often have communication deficits making self-report instruments inappropriate for this population. The first goal of this study further investigated the psychometric properties of The Scale for the Evaluation and Identification of Seizures, Epilepsy, and Anticonvulsant Side Effects-B (SEIZES-B), for the evaluation and identification of AED SE using third-party ratings. The second goal of this study examined SE profiles of the SEIZES-B of those taking AEDs, those not taking AEDs, and those without epilepsy taking antipsychotic medications. This study represents an essential step towards validating the use of this scale in the ID population and may facilitate its use in identifying SE from AED use. A brief review of ID, seizures and epilepsy, and those with comorbid ID and epilepsy is discussed.

Definition and Classification

Prior to the nineteenth-century there was little uniformity worldwide in the description and classification of ID. Although ID has always been present, its definition is socially and politically driven (Patton & Jones, 1994; Scheerenberger, 1983). The official classification of ID was formulated by two organizations, the American Association on Mental Retardation (AAMR; 1992) and the American Psychiatric Association (APA; 2000). The AAMR and APA classification system include three essential features of ID, including: 1) deficits in intellectual functioning; 2) concurrent deficits in adaptive functioning; and 3) onset before age 18. While these classification systems are similar on the basis of criteria used to determine ID, they differ in their application. For example, the AAMR definition is intended to facilitate inclusive education, supported or competitive employment, and supported living (MacMillian, Gresham, & Siperstein, 1995), whereas the Diagnostic and Statistical Manual, Fourth Edition Text Revision (DSM-IV-TR) specifies severity levels of ID based on standardized, individually administered intelligence tests (APA, 2000).

Assessment of Intellectual Functioning

General intellectual functioning is measured by the intelligence quotient (IQ; Eysenck, 1962), obtained by objective, standardized, individually administered intelligence tests (e.g., Standford-Binet, Wechsler Intelligence Scales; APA, 2000). In 1905, the Binet-Simon Individual Tests of Intelligence was the first intelligence test that assessed judgment, comprehension, reasoning, as well as, distinguished between varying degrees of ID (i.e., idiocy, imbecility, and moronity; Eysenck, 1962). Currently, sub-average intellectual functioning is defined as an IQ score of approximately 70 or below, which are two standard deviations below the population

mean (Biasini, Grupe, Huffman, & Bray, 2001). Until 1960, sub-average intelligence was considered the sole criteria for ID classification according to the AAMR (AAMR, 1992). In 1961, the AAMR redefined ID to also include limitations in adaptive functioning and onset before age 18 (Patton & Jones, 1994).

One of the major problems in applying conventional intelligence tests to the ID population is that these individuals may be influenced by additional deficits such as lack of motivation to comply with testing, thus making it difficult or impossible to use the available instruments and testing protocols (Beirne-Smith, Ittenbach, & Patton, 1994). Another criticism in applying conventional intelligence tests to this population is that intelligence tests measure a limited range of intellectual abilities. There are other abilities such as adaptive behavior, which rely on everyday (i.e., social and practical) intelligence that cannot be estimated accurately by standardized intelligence tests (Patton & Jones, 1994). To this end, adaptive functioning has become an important and necessary accessory to any diagnostic standard for ID (Greenspan, Switzsky, & Granfield, 1996).

Assessment of Adaptive Functioning

Assessment of adaptive behavior focuses on how well an individual can function independently and meet the social and practical demands imposed on the individual by their culture (Beirne-Smith, Patton, & Ittenbach, 1994). According to the DSM-IV-TR, criteria is met when deficits in at least two of the following 10 areas has been demonstrated: communication, social skills, self-care, home living, use of community resources, self-direction, health and safety, functional academics, leisure, and work (APA, 2000). Although there are numerous adaptive behavior scales, the most commonly used scale is the Vineland Adaptive Behavior Scales (VABS; Sparrow, Balla, & Cicchetti, 1984). The VABS was designed to assess

handicapped and non-handicapped persons from birth to adulthood in their personal and social functioning. The VABS is organized around four behavior domains: communication, daily living skills, socialization, and motor skills (Doll, 1953). The utility of adaptive instruments for identifying persons with ID has been debated because domains such as leisure, work, and use of community resources are difficult to define and measure (Zigler, Balla, & Hodapp, 1984). On the other hand, adaptive scales used in conjunction with other standardized assessments provide valuable information regarding communication, social skills, and daily living which can be useful in treatment planning (Greenspan, Switzsky, & Granfield, 1996).

The last criterion for a diagnosis of ID is onset before age 18 (AAMR, 1992; APA, 2000). For example, many chromosomal abnormalities associated with more severe levels of ID such fragile X syndrome or Down's syndrome is diagnosed during pregnancy or infancy (Dykens, Hodapp, & Fincucane, 2000). Milder levels of ID tend to be diagnosed in early childhood whereas ID with an unknown etiology is usually diagnosed later in childhood (Alexander, 1998).

Characteristics of Intellectual Disability

The current criteria used to differentiate severity levels of ID are associated with ranges of IQ scores. According to the DSM-IV-TR criteria, severity levels of ID are divided as follows: Mild (IQ level 50-55 to 70-75); Moderate (IQ level 35-40 to 50-55); Severe (IQ level 20-25 to 35-40); Profound (IQ level below 20 or 25); and Severity Unspecified (strong presumption of ID but the individual cannot be successfully tested by standardized intelligence tests).

The Mild group comprises about 85% of those classified as ID (APA, 2000). These individuals are often not physically distinguishable from those without ID. During infancy and early childhood, those with mild ID may have minimal impairment in social, communication

skills and sensorimotor functioning. By their late teens, learning difficulties may emerge in their academic work. During adulthood, these individuals typically live successfully in the community with minimal assistance, although some guidance may be necessary during stressful situations such as economic hardships (Harris, 1995).

The Moderate group comprises approximately 10% of those classified as ID (APA, 2000). Language development, social interactions, and communication skills vary across this group. Some have the capacity to have simple conversations while others have limited communication of basic needs (APA, 2000). These individuals also have limitations in their achievement of self-care and motor skills into adulthood. These individuals typically need supportive employment programs, supported workshops, and live in community-based group homes (Harris, 1995).

The Severe group comprises approximately 3% to 4% of the ID population (APA, 2000). These individuals typically have marked motor impairment and other associated deficits in language, communication, and self-care. These individuals typically need supervision in task performance in group homes or community programs (Harris, 1995).

The Profound group comprises approximately 1% to 2% of the ID population (APA, 2000). These individuals typically have neurological and physical disabilities that impair sensorimotor functioning and language comprehension. They may have limited understanding of simple verbal instructions and often require continual assistance with self-care. These individuals usually benefit from highly structured environments, such as developmental centers (Harris, 1995).

Lastly, the Severity Unspecified category is reserved for cases where there is a presumption of ID, but IQ values are unobtainable because the individual cannot be assessed by

standard tests. This may occur when children, adolescents, and adults are uncooperative or too impaired to participate in standardized testing (APA, 2000). These individuals typically have physical and sensory disabilities, such as blindness, deafness, and/or severe behavioral deficits (Harris, 1995).

Etiology of Intellectual Disability

The etiology of ID is based either on identifying a causative agent or a specific mechanism usually diagnosed in infancy or childhood (Harris, 1995). For example, many chromosomal abnormalities, including fragile X syndrome and Down's syndrome can be definitively diagnosed during pregnancy by chromosome analysis (Dykens, Hodapp, & Finucane, 2000). Developmental errors or teratogenic factors during prenatal, perinatal, and postnatal periods may increase the likelihood of developing ID (Alexander, 1998).

Developmental abnormalities during prenatal periods include chromosomal disorders, syndrome disorders, inborn errors of metabolism, and developmental disorders of brain formation. Elevated levels of alpha-fetoprotein for example, may increase the risk for neural tube defects and trisomy chromosomal aberrations during gestation (Crocker, 1992). In approximately 20% to 30% of those with severe ID, the cause has been attributed to prenatal factors (Dykens, Hodapp, & Finucane, 2000).

Developmental problems during perinatal periods may include intrauterine disorders and neonatal disorders. Perinatal factors such as hypoxia, hydrocephalus, and neonatal seizures account for approximately 11% of those with severe ID (Bernes & Kaplan, 1994). Lastly, postnatal causes typically include head injuries, infections, degenerative disorders, seizure disorders, toxic metabolic disorders, malnutrition, and environmental deprivation (Harris, 1995). Exposure to environmental toxins, such as lead and mercury, account for approximately 3% to

12% of those with severe ID (Dykens, Hodapp, & Finucane, 2000). Conversely, it has been estimated that between 45% and 63% of mild ID cases are attributed to unknown causes, and very few postnatal causes have been associated with mild ID (McLaren & Bryson, 1987).

Prevalence of Intellectual Disability

Over the past 100 years the prevalence of ID has been affected by changes in diagnostic criteria, empirical sampling, and improvements in medical care and technology (Sheerenberger, 1983). Based on empirical sampling, Baroff (1991) has suggested that only 0.9% of the population can be assumed to have ID. Following a review of epidemiological studies, McLaren and Bryson (1987) reported that the prevalence of ID was around 1.25% of the total population.

SEIZURES AND EPILEPSY

Classification and Diagnosis

Though there have always been people with seizures and epilepsy, the modern medical era of epileptology began during the late 19th century. A British neurologist, John Hughlings Jackson, defined seizures as an "occasioning, excessive and disorderly discharge of nerve tissue on muscles" and recognized their effect on consciousness, sensation, and behavior (Jackson, 1890, p. 703). Prior to 1929, diagnostic measures of seizure activity and epilepsy lacked reliability and validity, and relied heavily on direct observation. However, in 1929 technological advances allowed for concurrent electroencephalogy and filming of patient behavior. More recently, simultaneous EEG telemetry and video of concurrent behavior has refined our knowledge of the relationship between epileptiform abnormalities and observed behavior (Gastaut, 1970; Sundaram, Sadler, Young, & Pillay, 1999). Technology has greatly advanced the ability of medical professionals to identify and differentially diagnose neurological deficits; EEGs are now considered the gold standard among criteria for diagnosing epilepsy (Cuthill & Espie, 2005).

The most widely accepted classification system of seizure types and epileptic syndromes that is currently used is the International Classification of Epilepsies and Epileptic Syndromes (ICES). This classification system, proposed by the Commission on Classification and Terminology of the International League Against Epilepsy (ILEA) in 1989, defines an ictus (i.e., seizure) as a sudden neurological occurrence. Epilepsy is defined as a chronic neurological condition characterized by recurrent epileptic seizures (Gastaut, 1973). Epilepsy is differentiated from incidental seizures in that epilepsy is a chronic, long-lasting condition of at least two or

more seizures and predisposes individuals to have more seizures (Adams, Victor, & Ropper, 1997).

Epileptic seizures can be classified according to their etiology, clinical manifestation, and anatomic focus or source of origin. Epilepsy syndromes are defined by a cluster of features that include, but are not limited to, seizure type, age of onset, heredity of seizures, EEG findings, comorbid conditions, response to treatment, and prognosis for seizure control and remission (Coulter, 1993). In medical literature, seizures are typically classified into two types: generalized and partial (Wyllie, 1993).

Generalized Seizures

Generalized seizures usually have a unilateral focus that spreads to become generalized. These seizures are accompanied by a widespread electrical discharge involving both hemispheres. They are typically divided into tonic-clonic seizures, absence seizures, and other generalized seizures. Generalized tonic-clonic seizures are the most common epileptic manifestation of childhood neurological diseases (Holmes, 1997). These seizures typically involve somatosensory auras that may include visual, auditory, olfactory, and gustatory experiences prior to the onset of a seizure (Tuxhorn, 2005). During a tonic-clonic seizure, stiffening of extremities (tonic phase), rhythmic jerking of an extremity or the whole body (clonic phase), and loss of consciousness occur (Trimble, Ring, & Schmitz, 2000).

The second type of generalized seizures, absence seizures, are subtler than tonic-clonic seizures because they occur suddenly and are often mistaken for daydreaming. These individuals may appear to have a blank facial expression, suffer from loss of consciousness, and may have automatisms in the form of lip smacking, licking, chewing, and finger movements (Tuxhorn, 2005). Subtypes of absence seizures include typical and atypical. Typical absence seizures are

often very brief and involve loss of consciousness only. In contrast, atypical absence seizures last longer and may involve tonic, clonic, or automatic movements (Holmes, 1997). Although atypical absence seizures are characteristically similar to absence seizures, they are often associated with other types of seizures and are typically more difficult to control with antiepileptic medications (Schiff, Labar, & Victor, 1999).

Other generalized seizures include tonic, clonic, myoclonic, and atonic seizures. These seizures represent the least common types of generalized seizures (Adams, Victor, & Ropper, 1997). Unlike tonic-clonic seizures, tonic and clonic seizures occur independently but have tonic-clonic features such as loss of consciousness (Trimble, Ring, & Schmitz, 2000). Myoclonic and atonic seizures are differentiated from tonic and clonic seizures because loss of consciousness does not occur during these episodes (Mangano, Fontana, & Cusumano, 2005). Myoclonic seizures are characterized by single or repetitive contractions of a muscle or group of muscles, whereas atonic seizures are characterized by sudden, momentary loss of posture or muscle tone. Generalized myoclonic, atonic, and tonic seizures are all features of the Lennox-Gastaut syndrome common in the ID population. The Lennox-Gastaut syndrome is defined as the presence of slow-spike wave complexes in individuals with tonic seizures and more than one other seizure type (Aicardi & Gomes, 1988).

Partial Seizures

Unlike generalized seizures, partial seizures begin in a specific area of one cerebral hemisphere and do not spread bilaterally (Holmes, 1997). Partial seizures, which are associated with lesions of the temporal lobe (Schiff, Labar, & Victor, 1999), are subdivided into simple partial seizures (in which consciousness retained); and complex partial seizures (in which consciousness is impaired or lost) (Kotagal, Rothner, Erenberg, Cruse, & Wyllie, 1987). Both

simple and complex partial seizures are often accompanied by somatosensory auras, including complex visual or auditory hallucinations (Janszky, Schulz, & Ebner, 2004). Additionally, partial seizures may spread to cause a generalized seizure, in which case the classification category is partial seizures secondary generalized (Holmes, 1997).

Etiology of Epilepsy

According to the ICES (1989), there are three etiological classifications of epilepsy. These etiological classifications include confirmed, suspected, and unknown. Potential factors leading to the presence of epilepsy include a genetic predisposition, alternations in neuronal and neurotransmitter metabolism, electrophysiological abnormalities, and neuropathic changes (Adams, Victor, & Ropper, 1997). Additionally, there are certain etiological factors associated with age of onset. More specifically, in infancy and early childhood, chromosomal abnormalities, congenital disorders, metabolic disorders, and brain infections (e.g., encephalitis, meningitis), are considered to be the most common etiological factor (Okumura et al., 2000). In young adults, head trauma and brain tumors are the most common cause of seizures. In older adults, comorbid physical and neurological conditions (e.g., cerebrovascular disease, degenerative disease) are the most common cause (Gareri, Gravina, Ferreri, & De Sarro, 1999). Although numerous causes of epilepsy are known, it has been estimated that underlying causes of epilepsy is unknown in up to 50% of cases (Wyllie, 1993).

Prevalence of Epilepsy

Given the complex nature of classifying and diagnosing seizures and epilepsy, it is not surprising that prevalence rates vary. Possible explanations for this phenomenon include newly diagnosed cases of unprovoked seizures, the utilization of various diagnostic criteria in experimental settings, and lack of standardized definitions of seizure control (Mohanraj &

Brodie, 2005). Nevertheless, Hauser and Hesdorffer (1990) estimate that epilepsy affects approximately 1% to 3% of the general population. Further, these researchers suggest that approximately 1% of persons within the United States will have epilepsy by the age of 20.

Prognosis

Treatment outcome depends on the etiology of the epilepsy, the frequency, intensity, duration, and type of seizures. Seizures with particularly bad prognostic features include epilepsy associated with congenital neurological deficits, progressive neurological disorder, suspected or unknown etiology, partial epilepsies, and those with Lennox-Gastaut syndrome (Berg et al., 2001; Drislane & Schomer, 1994; Rantakallio, von Wendt, & Koivu, 1987). All of these conditions have particularly high associations with ID (Chevrie & Aicardi, 1978; Lennox, 1960; Koo & Holmes, 1999; Okumura, 2000; Yamanouchi et al., 2005).

Treatments

There are two types of treatments available for epilepsy: pharmacological and surgical. The first line of epilepsy treatment is pharmacological. This typically includes an AED regimen and therapeutic drug monitoring via laboratory testing of blood levels (Patil & Bodhankar, 2005; Specht, Elsner, May, Schimichowski, & Thorbecke, 2003). However, those who do not achieve satisfactory seizure control despite adherence to pharmacological interventions (i.e., refractory epilepsy) are often considered candidates for specific surgical interventions. Characteristics of good candidates for brain surgery include those with a distinct epileptic focus in a surgically removable area of the brain (e.g., lobectomy, hemispherectomy). Individuals with additive handicaps such as ID or multi-epileptic foci are often considered to be poor candidates for brain surgery (Wilfong, 2002). However, in individuals with refractory epilepsy and where removal of brain tissue is not feasible, these individuals are sometimes considered for vagal nerve

stimulation (VNS) surgery (Andriola & Vitale, 2001). The vagal nerve stimulator is an electrode that is surgically implanted around the left vagus nerve and normalizes electrical pulses to the brain (Gates, Huf, & Frost, 2001). The normalization of neuronal activity mitigates the frequency and severity of seizures in some individuals (Huf, Mamelak, & Kneedy-Cayem, 2005).

Pharmacological Treatment

Antiepileptic drugs are traditionally used in the treatment of epilepsy. There are two families of AEDs: classic and newer. Classic AEDs include phenobarbital, phenytoin, primidone, ethnosuximide, carbamazepine, benzodiazepines, and valproate (Herranz, Armijo, & Arteaga, 1988). Newer AEDs, which include oxcarbazepine, gabapentin, lamotrigine, and sabril, reportedly have less toxicity than classic AEDs with respect to the central nervous system (CNS; Harden, 1997).

Based on their psychotropic properties and mechanisms of action, classic and newer AEDs are generally classified as sedating or activating (McDonnell & Morrow, 1996). Sedating AEDs (e.g., barbiturates, benzodiazepines, valproic acid, gabapentin, tiagabine, and vigabatrin) are associated with fatigue, cognitive slowing, and possible anxiolytic and antimanic effects. These actions may be related to a predominance of potentiation of y-adminobutyric acid (GABA) inhibitory neurotransmission (Ketter, Post, & Theodore, 1999). Activating AEDs (e.g., felbamate and lamotrigine) have possible anxiogenic and antidepressant effects, such as agitation, aggression, irritability, and hyperactivity, and are associated with attenuation of glutamate excitatory neurotransmission (Reijs, Aldenkamp, & De Krom, 2004).

Although significant pharmacological advances have been made in the treatment of epilepsy, it is evident that none of the major AEDs are free from untoward side effects (SE; Brodie, 2001). There are generally five domains of SE individuals experience from AED use.

These domains include cognition, mood, behavior, motor, and physical effects (Gates, 2000; Glauser, 2004; Reijs, Aldenkamp & Krom, 2004). The most common SE of cognitive impairments includes decreased performance on intelligence tests, memory, attention, confusion, and processing speed (Drane & Meador, 2002). Side effects associated with both classic and newer AEDs include dizziness, abnormal vision, ataxia, tremors, hepatic toxicity, nausea, vomiting, gastrointestinal problems, alopecia, rash, and weight changes (Buchanan, 1992; Carpay, Aldenkamp, & van Donselaar, 2005).

Classification and Diagnosis

Similar to the diagnosis of epilepsy in the general population, a diagnosis of epilepsy in individuals with ID is based on patient history information (Richardsson, Koller, & Katz, 1981). Oftentimes the causative agent of ID is considered when diagnosing epilepsy in this population, as they often have a common etiology (Coulter, 1993). For example, prevalence studies indicate that 5% to 50% of individuals with mild and moderate ID have epilepsy and 30% to 70% with severe and profound ID have epilepsy (Coulter, 1993; Marcus, 1993; Pellock & Hunt, 1996). It is well established that there is a significant positive correlation between the incidence of epilepsy and severity of ID (Heller, 1969; Ieshima & Takeshita, 1988; Kumada et al., 2005; Marcus, 1993). For example, in a study of 1479 children and adults, Forsgren and colleagues (1990) found that 299 patients had comorbid ID and epilepsy. Of the 299 patients with ID and epilepsy, 14% had mild ID, 20.4% had moderate ID, 34.8% had severe ID, and 30.8% had profound ID. However, an important consideration is that reported rates differ between researchers.

Prevalence of Intellectual Disability and Epilepsy

Prevalence rates of epilepsy are much higher in children and adults with ID than in the general population (Corbett, Harris, & Robinson, 1975; Forsgren, Edvinsson, Blomquist, Heijbel, & Sidenvall, 1990; Ieshima & Takeshita, 1988; Kumada et al., 2005; McDermott, Moran, & Platt, 2005; Pary, 1993). Currently, the cumulative risk of epilepsy increases substantially in persons with ID if there are any co-morbid conditions such as cerebral palsy, movement disorders, cerebral injury, and degenerative CNS diseases (Amano et al., 2000; Cole, 2002; Goulden, Shinnar, Koller, Katz, & Richardson, 1991; Mariani, Gerini-Strambi, Sala, Erminio, & Smirne, 1993). Other risk factors for epilepsy in older-onset cases include

individuals with Down's syndrome, those with vascular disease, brain tumors, Alzheimer's syndrome, and multiple sclerosis (Wyllie, 1993).

In fact, rates of epilepsy have been estimated to be approximately 40% to 60% in institutionalized ID populations (Mattson, 1996). This increased rate is due to the fact that many individuals with ID have comorbid neurological disorders, as well as epilepsy. For example, approximately three to six children per 1000 births are afflicted with cerebral palsy, moderate or severe ID, or both (Steffenburg, Hagberg, &Kyllerman, 1996). Moreover, it has been estimated that one third of those with ID and cerebral palsy have epilepsy (Richardsson, Koller, & Katz, 1981).

Pharmacological Treatment

In the past decade there has been an emphasis on polypharmacy reduction and a shift from using classic AEDs to newer AEDs in the ID population (Bourgeois, 2001; Bennet, Dunlop, & Ziring, 1983; Ettinger, Barr, & Solomon, 2001; Kelly, Stephen, & Brodie, 2004; Mattson, 1996; Pellock & Hunt, 1996; Poindexter, Berglund, & Kolstoe, 1993). Research has shown that newer AEDs are better tolerated in those with ID and multiple handicaps (Pellock, 2002; Perucca, Beghi, Dulac, Shorvon, & Tomson, 2000). Despite this, polytherapy and classic AED use are still common practice in institutionalized ID populations because withdrawal of these drugs after long-term exposure may cause an increase in seizures (Genton, 2000; Goeckner, Rosenfeld, & Weber, 1995) or unmanageable behavior (Baumeister & Sevin, 1990; Clarke, Kelley, Thinn, & Corbett, 1990; Kerr, 2002; Matson et al., 2000), even when appropriate AEDs are prescribed and blood levels are in their therapeutic ranges (Patil & Bodhankar, 2005; Specht, Elsner, May, Schimichowski, & Thorbecke, 2003). For example, Pellock and Hunt (1996) conducted an open 10-year study with 244 individuals with ID and epilepsy. These

researchers found that in this sample the most frequently administered AEDs were phenobarbital (69%), phenytoin (21%), primidone (8%), and carbamazepine (1%). Similar patterns of AED use have been documented in other studies (Matson, Mayville, & Bamburg, 2001; Mattson, 1996; Pellock, 2002).

Barbiturates

Barbiturates are generalized CNS depressants and have historically been regarded as the first choice in treating recurrent seizures (Porter & Melldrum, 1990). Common barbiturates include phenobarbital and primidone and are used to treat generalized tonic-clonic seizures and partial seizures (Vinning, Carpenter, & Aman, 1999; Pellock, 2002). Phenobarbital and primidone modulates GABA at the postsynaptic receptor (Porter & Meldrum, 1990). Common SE of phenobarbital and primidone include sedation, rash, ataxia, and disturbances of cognition, mood, and behavior (Rogvi-Hansen & Gram, 1995; DeToledo, Lowe, & Haddad, 2002; Pellock & Hunt, 1996). Phenobarbital also induces hepatic microsomal metabolism; thus, the likelihood for drug interactions is extremely high when it is used as co-therapy (Patsalos & Perucca, 2003). One of the most commonly reported SE in the general population is drowsiness (Harbord, 2000). Although barbiturates have sedating effects, hyperactivity and irritability are frequently observed in those with ID (Glauser, 2004; Goeckner, Rosenfeld, & Weber, 1995; Pellock, 2002). Given the severity of these SE in the ID population, barbiturates are becoming less frequently used and are generally reserved for those with refractory epilepsy (Pellock, 2002).

Phenytoin

Historically, phenytoin has been a first-line medication for the prevention of tonic-clonic seizures, partial seizures, and acute seizure management (i.e., status epilepticus) (Pellock, 2002). Phenytoin blocks sustained high-frequency repetitive firing of action potentials by altering

sodium, potassium, and calcium conduction of membrane potentials (Porter & Meldrum, 1990). Unlike phenobarbital, phenytoin is one of the best-tolerated AEDs in the general population and does not have sedative effects (Porter & Meldrum, 1990). In the ID population however, serious neurological damage has been associated with phenytoin, such as deterioration of cognitive functioning and ataxia (Iivanainen, 1998). In addition, Matson et al., (2004) found that phenytoin use was associated with significant deficits in social skills in the ID population. Less serious SE of phenytoin includes cosmetic SE, such as gingival hyperplasia and hirsutism, which are more prevalent after chronic administration, higher doses, and polypharmacy (Buchanan, 1992; Pellock, 2002).

Carbamazepine

Carbamazepine has gained acceptance as a first-line treatment for tonic-clonic seizures, partial seizures (Waisburg & Alvarez, 1998), and secondary generalized seizures in those with ID, as well as comorbid psychiatric disease (Kanner, 2002; Pellock, 2002). The mechanism of action is similar to phenytoin, it acts pre-synaptically to decrease synaptic transmission but does not influence GABA uptake (Porter & Meldrum, 1990). Side effects of carbamazepine are similar to that of phenytoin (Herranz, Armijo, & Arteaga, 1988), including drowsiness, irritability, nausea and vomiting, nystagmus, and hepatic failure (Gates, 2000). However, due to its minimal SE on cognition and behavior, carbamazepine is widely used in persons with ID (Alvarez, Besag, & Iivanainen, 1998; Matson, Luke, & Mayville, 2004).

Valproate

Valproate, in the form of valproic acid or salt, is a broad-spectrum AED. It reduces the incidence and severity of tonic–clonic, absence, myoclonic, and partial seizures. It is frequently used in the ID population because those with one or more seizure type are often responsive to

valproate and suffer from relatively few SE with respect to cognition and behavior (Friis, 1998). Like phenytoin and carbamazepine, valproate blocks high-frequency repetitive firing of neurons at therapeutically relevant concentrations (Porter & Meldrum, 1990). Common SE include weight gain, tremor, hyperactivity, drowsiness, alopecia, and gastrointestinal upset (Buchanan, 1992; Gates, 2000). Although valproate may have moderate SE in some individuals, it continues to be administered in the ID population because of its efficacy against refractory epilepsy and its utility in mitigating comorbid behavioral aberrations such as impulsive-aggressive behavior (Gates, 2000; Pellock, 2002; Rutecki & Gidal, 2002).

Benzodiazepines

Benzodiazepines are used primarily for status epilepticus and refractory epilepsy, which are common in the ID population (Lombroso, 1983; Pellock, 2002). There are six benzodiazepines that include clonazepam, lorazepam, and diazepam, clorazepate, midazolam, nitrazepam, and clobazam. Clonazepam and clorazepate are used for chronic treatment, whereas diazepam is used in the treatment of status epilepticus. Clonazepam is also used for absence, myoclonic, and atonic seizures where control with other drugs is difficult (Vinning, Carpenter, & Aman, 1990). All benzodiazepines have sedative properties that include drowsiness, somnolence, and fatigue (Gates, 2000). Benzodiazepines are generally not preferred because of the relatively high frequency of SE on cognition, mood, and behavior (Wyllie, 1993).

Lamotrigine

Lamotrigine has been indicated for treatment of generalized tonic-clonic seizures and partial seizures. Lamotrigine inhibits glutamate and aspartate release, blocks sodium channels, and prevents repetitive firing or neurons. It is chemically unrelated to other AEDs and is therefore commonly used as adjunctive therapy in adults. However, individuals with ID treated

with lamotrigine are at risk of experiencing Sturge-Johnson syndrome, a severe rash that can be irritating or fatal when combined with valproate (McKee et al., 2003). Other less severe SE from lamotrigine includes dizziness, headache, ataxia, somnolence, and hematologic abnormalities (Kustra et al., 2005).

Assessment of Antiepileptic Side Effects

Susceptibility to SE is inherent in all medications, especially in populations that experience long-term use (Clarke, Kelley, Thinn, & Corbett, 1990; Stein & Strickland, 1998). It has been estimated that approximately 25% to 30% of those with epilepsy in the general population will experience a recurrence of seizures despite appropriately prescribed medications and blood levels in therapeutic ranges (Patil & Bodhankar, 2005; Specht, Elsner, May, Schimichowski, & Thorbecke, 2003). This recurrence rate is even greater (i.e., 40%) in those with multiple handicaps, including ID (Singh & Towle, 1993). As a result, individuals with ID, especially those in institutionalized environments often experience long-term AED use because withdrawal from these drugs has been shown to increase seizures (Alvarez, Besag, Iivanainen, 1998; Pellock & Morton, 2000).

Despite the long history of AED availability and research on their efficacy, individual differences in clinical response and inconsistent research methodologies confound efforts to achieve a broad consensus regarding their psychoactive effects (Brodie, 2001; Chadwick, 1997; Harbord, 2000; McDonnell & Morrow, 1996; Meldrum, 2002; Mohanraj & Brodie, 2005; Perucca, 2002; Stein & Strickland, 1998). Selecting a specific AED for seizure treatment in those with ID requires a balance of the drug's likely efficacy for both seizures and comorbid disorders and minimizing SE (Perucca et al., 2000). In both the general and ID population, SE may be

tolerated or heightened, producing toxicity that may require dosage reductions (Alvarez, Besag, & Iivanainen, 1998; Matson, Mayville, & Bamburg, 2001; McKee, et al., 2003).

Assessing SE of AEDs in the ID population, however, poses considerable challenges not experienced in the general population (Alvarez, 1989). For example, information used to assess SE of AEDs in individuals with epilepsy is typically gathered by self-report, interviews, and direct observations (Mayville & Matson, 2004). However, individuals with ID and epilepsy generally have significant cognitive deficits and are frequently non-verbal, thus making self-report measures or interviews with the patient ratings inappropriate. These factors contribute to the complexity of assessment, treatment, and monitoring of SE in this population (Matson, Bielecki, Mayville, & Matson, 2003).

Given the limitations of patient self-report with this population, informant-based ratings scales, direct observations, and laboratory monitoring have become the primary method of assessing seizure activity and SE in these individuals (Mayville & Matson, 2004). Although some standardized measures on SE of AEDs in the general population exist (Kane, Lee, Bryant-Comstock, & Gilliam, 1996), research on SE of AEDs in institutionalized ID population is sparse and lacks systematic, reliable, and valid measures (Matson et al., 2000; Mayville & Matson, 2004). However, a recent study assessing the reliability of the SEIZES-B, designed to measure SE specific to AED use in the adult ID population, indicated moderately high overall inter-rater reliability (r = .72) and moderately high overall test-retest reliability (r = .63) (Matson, Laud, González, Malone, & Swender, 2005). The SEIZES-B scale addresses observable SE, as opposed to other scales that estimate subjective ratings of SE such as quality of life. The current study aims to further examine the psychometric properties of the SEIZES-B.

STUDY ONE

Rationale

Presently, there is a lack of research on standardized measures assessing SE of AEDs in individuals with ID and epilepsy. To date, no research has been conducted on the convergent validity of two measures assessing SE of AEDs in this population. Since this population is medically fragile, standardized measures assessing SE of AEDs are needed. Effectively monitoring SE of AEDs may allow medical professionals to adjust dosages, especially when multiple medications are in use. The purpose of this study was to further investigate the psychometric properties of the SEIZES-B. The current study's purpose had two goals. First, interrater reliability of direct observations using the Pinecrest Developmental Center (PDC) Nursing Assessment Form was explored. A licensed epileptologist and registered nurse served as the observers. Second, as direct observations and third-party report are the gold standards available for this population (Cramer & Mattson, 1993; Mayville & Matson, 2004), the epileptologist's direct observation ratings from the PDC Nursing Assessment Form was the standard against which the SEIZES-B was compared. This comparison served as a measure of convergent validity.

Method

Participants

Participants were resident patients of PDC in central Louisiana. PDC is a state-run residential community that provides 24-hour care to approximately 550 individuals with varying levels of ID, ages, genders, and races. An on-site licensed psychologist or board certified psychiatrist diagnosed all participants with ID based on DSM-IV-TR criteria (e.g., deficits in

intellectual and adaptive functioning before 18 years of age). Approval from the PDC Institutional Review Board (IRB) was obtained prior to data collection.

A power analysis was conducted to determine the sample size of the group required for the present study. The recommended level of power was set at .80, because alpha (α) or the predetermined level of significance was set at .05 (Cohen, 1988). Using GPOWER (Faul, & Erdfelder, 1992), a statistical program for determining power levels, it was determined that a total sample of 82 participants would be required to obtain significance for variance-based statistics at the .05 level.

Seventy nine individuals with varying levels of ID were recruited for inclusion in this study. During the course of data collection, six participants were removed from data analysis due to missing Nursing Assessment Form ratings from the epileptologist, leaving 73 participants. Participants included 43 males and 30 females diagnosed with mild (n = 1), moderate (n = 1), severe (n = 11), profound (n = 59), and unspecified (n = 1) ID. Of these participants, the majority were Caucasian (n = 51), with a smaller sub-sample of African Americans (n = 21), and a small sample identified as other (n = 1). Participants' ages ranged from 25 to 89 years, with an average age of 49 years. Demographic information is presented in Table 1.

Diagnosis of epilepsy was made by a consulting licensed neurologist who reviewed patient medical histories prior to data collection. Classification of seizure type, determined by the neurologist, was based on the ILEA criteria, clinical description of seizure activity, EEG pattern, and additional medical information (e.g., family history, age of onset, prior neurological trauma). Individuals who were excluded from participating in this study were those with: 1) non-epileptic seizures and, 2) no seizure activity for the past two years.

Table 1
Demographic Characteristics of Participants

Characteristic	*n*	%
Age at time of survey (years)		
0-21	1	1.4
22-45	32	44.5
46-65	31	43.1
66+	9	12.3
Gender		
Female	43	58.9
Male	30	41.1
Race		
Caucasian	51	69.9
African American	21	28.8
Other	1	1.4
Level of Mental Retardation		
Mild	1	1.4
Moderate	1	1.4
Severe	11	15.1
Profound	59	80.8
Unspecified	1	1.4

Of the 73 participants with ID and epilepsy, five seizure types were noted in the sample. The majority of the participants had partial epilepsy (*n* = 56), with 11 evolving into generalized seizures (i.e., partial seizures secondary generalized). Other seizure types included generalized (*n* = 6), Lennox-Gastaut (*n* = 7), and epilepsy NOS (*n* = 4). These diagnoses were noted during the chart review and are listed in Table 2.

Table 2
Classification of Seizure Types

Classification	*n*	%
Generalized	6	8.2
Partial	45	61.6
Partial seizures secondary generalized	11	15.1
Lennox-Gastaut	7	9.6
Epilepsy NOS	4	5.5

Since dosage and regimen of medications may have an impact on the presence and severity of SE, current medication use was noted during the participants' chart review. All participants were on at least one AED at the time of review. Twenty seven participants (37%) were on one AED, 29 participants (39.7%) were on two AEDs, 16 participants (21.9%) were on three AEDs, and one participant (1.4%) was on four AEDs. Overall, the use of classic AEDs (95.9%) versus newer AEDs (82.19%) did not differ substantially. See Table 3.

Table 3
Medication Usage

Frequency Count	*n*	%
Classic AEDs		
Carbamazepine	17	23.2
Clonazepam	3	4.1
Diastat	21	28.8
Diazepam	2	2.7
Lorazepam	1	1.4
Phenobarbital	1	1.4
Phenytoin	7	9.6
Primidone	2	2.7
Valproic Acid	16	21.91
Newer AEDs		
Gabapentin	1	1.4
Lamotrigine	24	32.9
Levetiracetam	10	13.7
Oxcarbazepine	5	6.9
Pregabalin	13	17.8
Topiramate	2	2.7
Zonisamide	5	6.9

Measures

The Scale for the Evaluation and Identification of Seizures, Epilepsy, and Anticonvulsant Side Effects B (SEIZES-B).

The SEIZES-B is a 52-item informant based instrument designed to measure SE specific to AED use in adults with ID and epilepsy. According to symptom severity, the informant rates items on a four-point Likert-type scale. The scale addresses the following topics which map onto 14 subscales that cover features of adverse SE from AED use: 1) Hematological Disturbances, 2) Electrolyte Disturbances, 3) Hepatic Disturbances, 4) Weight Disturbances, 5) Respiratory Disturbances, 6) Gastric Disturbances, 7) Dermatological Changes, 8) Hair Changes, 9) Gait Disturbance, 10) Tremor, 11) Sedation, 12) Affective disturbances (e.g., depression, tension/agitation anger/hostility), 13) Cognitive disturbances (e.g., decreased concentration and attention), and 14) Drug-related Dizziness (e.g., gait/movement disturbances).

Symptom severity is rated as follows: a score of ‘0’ indicates no disturbance; a score of ‘1’ indicates mild problems; a score of ‘2’ indicates moderate problems; whereas a score of ‘3’ indicates impairment in everyday functioning. Only one item from each subscale may be endorsed since items are rated on a continuum of increasing severity, with the exception of the following four subscales; 1) Gastric Disturbances, 2) Dermatological Disturbances, 3) Hair Changes, and 4) Sedation. These four subscales may have more than one item endorsed since multiple symptoms may be experienced. For example, in the gastric subscale, endorsement of item 19a, “Vomiting shortly after medication is given” may be experienced concurrently with endorsement of item 19b, “Vomiting throughout the day”. The endorsement of item 19a would yield a score of ‘2’ and endorsement of item 19b would yield a score of ‘3’. Therefore, the total item score for the gastric subscale would equal ‘5’.

The total score for each endorsed item is recorded in the corresponding numbered item space on Section B of the SEIZES-B scoring sheet. The number representing the total item score for each subscale is then circled on the scoring scale located above the individual item endorsement section and yield s a SEIZES-B profile.

Direct Observation Method. Direct observations of behavior were completed using the PDC Nursing Assessment Form. The PDC Nursing Assessment Form covers 15 physiological and psychosocial domains designed to closely monitor each patient. The PDC epileptologist and neurologists do not typically complete the Nursing Assessment Form. A registered nurse, with a background in neurology and psychopharmacology, completes the form after each neurology clinic visit. The assessment takes approximately 10 minutes to complete. The 15 domains include: 1) Vital Signs, 2) Level of Consciousness/Cognition, 3) Reaction to Stimulus (e.g., change in response to stimuli, extremity movement, general withdrawal, tremor), 4) Psychosocial (e.g., cooperation, restless/anxious, irritable, hostile/uncooperative), 5) Eyes, Nose, Throat, Sleep Patterns, Rest Patterns, 6) Cardiovascular (e.g., apical pulse, radial pulse, pedal pulse), 7) Respiratory (e.g., breath sounds, character of respirations, muscular contractions/reactions, cough sputum), 8) Gastrointestinal (e.g., bowel sounds, abdomen), 9) Bowel (e.g., stools, color of stools), 10) Renal Appearance, 11) Musculoskeletal (e.g., locomotion, balance, edema), 12) Skin (e.g., color, temperature, turgor, condition), 13) Dental (e.g., oral hygiene rating), 14) Reproductive System (e.g., masses, dimpling, discharge), and 15) Seizures (e.g., activity, acute episode, post-ictal state, VNS, any changes in seizure type, frequency, and duration). Spaces are provided next to each domain to record an absence or presence of symptoms. A blank box indicates an absence of symptoms whereas a checkmark in the box indicates the presence of symptoms.

Procedure

Participants were seen at the PDC neurology clinic each week for a period of two months. Prior to each visit, the nurse and epileptologist were given the PDC Nursing Assessment Forms. These forms were attached to the participant's medical chart. The nurse and epileptologist were instructed to directly observe the participant and complete the form independently for those that attended clinic. After the forms were completed, a list of participants that attended clinic that week was complied. The SEIZES-B was then administered for those participants who came into clinic that week. This control measure was taken in order to avoid time-order confounding effects.

Administration of the SEIZES-B was conducted by a bachelors-level clinical psychology graduate student. The graduate student served as the interviewer. The interviewer was trained specifically in the administration and scoring of the SEIZES-B before data collection began. Interviews took place in a quiet area of the participants' homes and took approximately 10 minutes to complete. Direct-care staff members who had known the participant for at least six months prior to the study served as informants. Each item was read to the direct-care staff members verbatim. Upon completion of the item, the interviewer instructed the direct-care staff to provide a rating. Information from the first four subscales of the SEIZES-B was collected from the participants' medical records by the interviewer. However, this information was not included in the analysis.

In order to estimate convergent validity, eight subscales of the SEIZES-B were compared to the corresponding items of the PDC Nursing Assessment Form. Subscales from the SEIZES-B that corresponded with the domains from the Nursing Assessment Form included: 1) Respiratory Disturbances, 2) Gastric Disturbances, 3) Dermatological Disturbances, 4) Gait Disturbances, 5)

Tremor, 6) Sedation, 7) Affective Disturbances, and 8) Cognitive Disturbances. Items from the PDC Nursing Assessment Form that did not overlap or could not be observed during the clinic visit with the SEIZES-B were not utilized in the comparisons (e.g., Hair Changes, Drug Related Dizziness, Sleep and Rest Patterns).

Results

Interrater Reliability of the Direct Observation

Interrater reliability of the direct observation using the PDC Nursing Assessment Form was calculated using Cohen's kappa correlation coefficient (κ) in order to measure agreement between dichotomous variables (presence versus absence of symptoms) while removing chance agreement (Hinkle, Wiersma, & Jurs, 1998). This was used to assess whether the nurse and epileptologist's ratings were consistent between observers. Results revealed that the highest individual item kappa correlation was $\kappa = .53$, $p<.05$ for Alert/Awake. However, overall, the majority of the items reflected low positive correlations (Hinkle, Wiersma, & Jurs, 1998). For example, 5 out of the 14 correlations fell below $\kappa = .00$. In addition, for a number of items no statistics could be computed because the variable was a constant (e.g., shallow breathing, deep breathing, emesis, rash, and excoriated skin). The individual item interrater reliability of the direct observation is shown in Table 4.

Table 4
Interrater Reliability of the Direct Observation

Domain	κ
Respiratory	
Regular Respiration	-.02

(table continued)

(table continued)

Gastrointestinal	
Guarding	-.01
Skin	
Normal Color Skin	-.02
Pale Color Skin	.02
Musculoskeletal	
Gait Steady	.44
Change in Gait/Balance	.31
Reaction to Stimulus	
Intermittent Tremor	-.06
Frequent/Constant Tremor	.25
Psychosocial	
Irritable	.48
Hostile/Uncooperative	.25
Levels of Consciousness/Cognition	
Alert/Awake	.53
Sedated/Drowsy	.30
Lethargic	.25
Change in Cognitive Functioning	-.01

Convergent Validity of the SEIZES-B

Concordance between the SEIZES-B and direct observation were calculated using Pearson-product moment correlation coefficients (Tabachnick & Fidell, 2001). The results of the correlational analyses were not statistically significant for five of the following domains: Gastric Disturbances, Dermatological Disturbances, Tremor, Affective Disturbances, and Cognitive Disturbances. The correlation coefficients of the individual items ranged from -.06 for tremor, to .97 for Gait Disturbance. However, some of the participants were non-ambulatory; therefore this item was only calculated for a subset of the sample. Concordance between items of the SEIZES-B and direct observation yielded a very high positive correlation for Gait Disturbance, r =.97, p<.001 and low positive correlation for Sedation, r =.26, p<.05. Most of the correlation coefficients could be classified as having low positive to little if any clinical significance (Hinkle, Wiersma, & Jurs, 1998). No statistics were available for Respiratory Disturbance because the variable on the PDC Nursing Assessment Form was a constant. Concordance rates for the SEIZES-B and direct observation are presented in Table 5.

Table 5
Corresponding Total Subscale Scores of the SEIZES-B and Direct Observation

SEIZES-B	Nursing Assessment Form	*r*
Respiratory Disturbance	Respiratory	--
Gastric Disturbances	Gastrointestinal	-.02
Dermatological Disturbances	Skin	-.03
Gait Disturbances	Musculoskeletal	.97***

(table continued)

(table continued)

Tremor	Reaction to Stimulus	-.06
Sedation	Level of Consciousness/Cognition	.26*
Affective Disturbances	Psychosocial	.21
Cognitive Disturbances	Level of Consciousness/Cognition	-.01

-- unable to calculate due to lack of variance

*** $p < .001$

* $p < .05$

STUDY TWO

Rationale

The purpose of this study was to investigate differences in the baseline level of symptomatology across individuals with ID. Three groups, comprised of those with epilepsy taking AEDs, those with a diagnosis of epilepsy not taking AEDs, and those without epilepsy taking antipsychotic medications were compared. Individuals without epilepsy taking antipsychotic medications served as the control group to determine if significant differences in the baseline level of such symptoms existed. Based on the available research (Alvarez, Besag, & Iivanainen, 1998; Brodie, 2001; Ettinger, Barr, & Solomon, 2001; Gates, 2000), it was hypothesized that those with epilepsy taking AEDs would have higher SE ratings than those not taking AEDs and those taking antipsychotic medications because the SEIZES-B was developed to assess SE specific to AED use. The relationship between the baseline level of SE symptoms in those taking AEDs, non-AEDs, and anti-psychotics has not been researched in the literature.

Following the comparison across the three groups for overall SE profiles, a series of item correlation coefficients within ten subscales of the SEIZES-B was conducted. This analysis was exploratory and indicated whether a relationship existed between specific items of the SEIZES-B across the designated groups.

Method

Participants

Participants were recruited from PDC in central Louisiana. Individuals participating in this study were those with a diagnosis of ID.

A power analysis was conducted to determine the sample size of the groups required for the present study. Using GPOWER (Faul & Erdfelder, 1992) with a predetermined level of

significance set at .05 (Cohen, 1965; 1988), it was determined that a total sample of 159 participants was required for an ANOVA with three groups for a medium effect size (.5). The present study only had 15 participants in each group, with a total sample size of 45. While this small sample size serves as a limitation of this study, the study remains important given the importance of this topic.

Three groups of individuals with ID participated in this study. They included individuals with epilepsy taking AEDs (n = 15), individuals with a diagnosis of epilepsy not taking AEDs (n = 15), and individuals without epilepsy taking antipsychotic medications (n = 15). Participants were matched across groups for age (within 10 years), gender, race, level of ID, seizure type (where appropriate), and medication type to prevent confounding effects these variables might produce prior to data collection. Categorical variables like gender, race, level of ID, seizure type, and number of psychotropic medications, were compared using chi-square analysis. Based on these analyses, there were no significant differences in these variables.

Age, a continuous variable, was compared using a one-way ANOVA. Based on this analysis, there were no significant differences in age. Participants' ages ranged from 26 to 87 years, with the average age of 52 years. There were 34 males and 11 females with mild (n = 0), moderate (n = 7), severe (n = 12), profound (n = 25), and unspecified (n = 1) ID. The majority of the participants were Caucasian (n = 33) and a smaller sub-sample were African American (n = 12). Demographic information is presented in Table 6.

Diagnosis of epilepsy was made by a consulting neurologist who reviewed patient medical histories prior to data collection. Classification of seizure type, determined by the neurologist, was based on ILEA criteria, clinical description of seizure activity, EEG pattern, and additional medical information. These diagnoses were noted during the chart review.

Table 6
Demographic Characteristics of Groups

Characteristic	AED (*n* = 15)	Non-AED (*n* = 15)	Control (*n* = 15)
Age			
0-21	0 (0%)	0 (0%)	0 (0%)
22-45	7 (46.7%)	3 (20.0%)	7 (46.7%)
46-65	6 (40.0%)	9 (60%)	5 (33.3%)
66+	5 (33.3%)	3 (20.0%)	3 (20.0%)
Gender			
Female	11 (73.3%)	11 (73.3%)	11 (73.3%)
Male	4 (26.7%)	4 (26.7%)	4 (26.7%)
Race			
Caucasian	11 (73.3%)	11 (73.3%)	11 (73.3%)
African American	4 (26.7%)	4 (26.7%)	4 (26.7%)
Level of ID			
Moderate	2 (13.3%)	3 (20.0%)	2 (13.3%)
Severe	4 (26.7%)	4 (26.7%)	4 (26.7%)
Profound	9 (60.0%)	7 (46.7%)	9 (60.0%)
Unspecified	0 (0%)	1 (6.7%)	0 (0%)

Of the 30 participants with ID and a diagnosis of epilepsy (AED and non-AED group), there were four seizure types noted in this sample. The majority of the participants had generalized epilepsy (n = 18), eight had partial epilepsy (v = 3), five out of those eight evolving into secondary generalized seizures (n = 5), and Epilepsy NOS (n = 4).

Differences in medication may have an impact on the presence and severity of symptoms. Current medications were noted during the participant's chart review. All participants in the AED and control group were on medications. In the AED group, it was found that 73.3% were on one AED, while 20% were taking two AEDs, and 6.7% were taking three AEDs. In the non-AED group, none of the participants were taking psychotropic medications. In the control group, the majority of participants (93.3%) were only on one psychotropic medication, while only one participant was on two (6.7%).

Games-Howell post hoc analyses were employed because equal variances were not assumed between groups (Hinkle, Wiersma, & Jurs, 1998). According to the post hoc analyses, no significant differences between the three groups on age, visual impairments, hearing impairments, and verbal ability (verbal or non- verbal) were identified. Seizure type between the AED group and non-AED did not significantly differ. However, significant differences were found in ambulation and medication usage among the three groups. That is, significantly more participants in the control group were ambulatory (93.3%) than in the AED group (46.7%), $F(2, 42) = 5.15$, $p = .014$. In addition, a significant difference was found in medication usage among the three groups, $F(2, 42) = 21.10$, $p = .00$. That is, significantly more participants in the AED group ($p = .00$) and control group ($p = .00$) were taking medications than the non-AED group ($p = .00$). However, differences in the amount of medication taken between the AED group and

control group was non-significant (p = .29). Table 7 shows the frequency of medication usage among the three groups at the time of the chart review.

Table 7
Medication Usage of the Groups

Medication Class	Frequency of Usage		
	AED (n = 15)	Non-AED (n = 15)	Control (n = 15)
Classic AEDs			
Carbamazepine	2	0	0
Diastat	2	0	0
Phenytoin	5	0	0
Valproic Acid	4	0	0
Newer AEDs			
Lamotrigine	5	0	0
Zonisamide	1	0	0
Anti-psychotics			
Aripiprazole	0	0	3
Olanzapine	0	0	5
Quitiapine	0	0	2
Risperidone	0	0	4
Thioridazine	0	0	1
Anxiolitic			
Propanolol	0	0	1

Measures

The SEIZES-B, as previously discussed in Study One, is a 52-item informant based scale developed for use with adults with ID and epilepsy.

Procedure

The SEIZES-B was administered to direct-care staff members that had known the participant for a minimum of six months prior to the study. A bachelors-level clinical psychology graduate student served as the interviewer. Information from the first four subscales of the SEIZES-B in the AED group was collected from the individual's chart or medical records by the interviewer. However, this information was not utilized in the comparison. Interviews were conducted in accordance with the SEIZES-B manual specifications. All data was collected in the same two-month period to prevent confounding effects of time.

Following the comparison of the three groups on SE profiles, a series of item correlation coefficients were conducted for the following ten subscales from the SEIZES-B: 1) Respiratory Disturbance, 2) Gastric Disturbance, 3) Dermatological Disturbance, 4) Hair Changes, 5) Gait Disturbance, 6) Tremor, 7) Sedation, 8) Affective Disturbances, and 9) Cognitive Disturbance, and, 10) Drug-Related Dizziness.

Results

Total scores derived from the SEIZES-B were analyzed across the three diagnostic groups (AEDs, non-AEDS, control) using a one-way Analysis of Variance (ANOVA). Differences across the nine of the ten subscales of the SEIZES-B were all non-significant. However, a significant difference was found across the Hair Changes subscale $F(2, 42) = 3.50$, $p = .03$. With Games-Howell post hoc analyses, no significant difference was found between the AED group and control group ($p = .18$). Results are displayed in Table 8.

Table 8
Means, Standard Deviations, and ANOVA for SEIZES-B Subscale Totals

Variable	AED		Non-AED		Control		ANOVA	
	M	SD	M	SD	M	SD	*F*(2,42)	*p*
Respiratory Disturbance	.33	.90	.00	.00	.00	.00	2.05	.14
Gastric Disturbance	.40	.91	.27	.79	.00	.00	1.27	.29
Dermatological Disturbance	.33	.61	.40	.63	.21	.41	.49	.61
Hair Changes	.60	1.24	.00	.00	.00	.00	3.50	.03*
Gait Disturbance	.40	.91	.13	.51	.20	.41	.68	.51
Tremor	.13	.35	.00	.00	.00	.00	2.15	.12
Sedation	.27	.70	.27	.70	.13	.51	.21	.81
Affective Disturbance	.20	.56	.13	.51	.20	.56	.07	.92
Cognitive Disturbance	.00	.00	.07	.25	.13	.51	.60	.55
Drug-Related Dizziness	.07	.25	.00	.00	.00	.00	1.00	.37

*$p \leq .05$

After comparing the total subscale scores of the SEIZES-B across the three groups, item correlation coefficients were calculated using a matrix of Pearson product-moment correlation coefficient. Each item within the ten subscales of the SEIZES-B was compared across the three groups. Since this analysis was exploratory in nature, a two-tailed test of significance was set because the direction of the relationship was unknown. Based on this analysis, six of the ten subscales contained items that were significant in the AED group.

In the AED group, very high positive correlations were observed for vomiting shortly after medication is given and unsteady wide based gait, $r = 1.0$, $p<.01$, vomiting shortly after medication is given and transient dizziness, $r = 1.0$, $p<.01$, vomiting throughout the day and transient dizziness, $r = 1.0$, $p<.01$, can only walk with assistance and some mood change; no interference with daily activities, $r = 1.0$, $p<.01$, and mood changes, interference with some activities and unsteady wide based gait, $r = 1.0$, $p<.01$. In addition, the non-AED group had moderate to very high positive correlations. The control group had two moderately high correlation coefficients. Overall, the majority of the correlation coefficients were in the low to moderate range. Only significant correlations and are presented in Table 9.

Table 9
Pearson Product-Moment Correlation Coefficient for SEIZES-B Items Across Groups

Subscale and Item	Item	*r*
AED Group		
Respiratory Disturbances		
Shortness of breath	Slow, unsteady gait	.48**
Labored Breathing	Intermittent tremor	.63**
Gastric Disturbances		
Vomiting shortly after medication is given	Unsteady, wide based gait	1.0**
Vomiting shortly after medication is given	Intermittent tremor	.68**
Vomiting shortly after medication is given	Some mood changes; no interference with tasks	.68**

(table continued)

(table continued)

Vomiting shortly after medication is given	Transient dizziness	1.0**
Vomiting throughout the day	Transient dizziness	1.0**
Vomiting throughout the day	Skin sensitive to light	.68**
Vomiting throughout the day	Hard to awaken, occasionally sleeps during the day	.68**
Dermatological Disturbance		
Rash consisting of red discolored patches	Hard to awaken, occasionally sleeps during the day	.65**
Rash consisting of red discolored patches	Difficult to stay awake especially during the day	.68**
Gait Disturbances		
Can only walk with assistance	Mood changes; interfere with some daily activities	1.0**
Tremor		
Intermittent Tremor	Unsteady wide based gait	.68**
Intermittent Tremor	Transient dizziness	.68**
Frequent or constant tremor	Hard to awaken, occasionally sleeps during the day	.68**
Sedation		
Some mood changes; no interference with activities	Unsteady wide based gait	.68**
Some mood changes; no interference with activities	Transient dizziness	.68**

(table continued)

(table continued)

Mood changes; interference with some activities	Unsteady wide based gait	1.0**
Non-AED Group		
Dermatological Disturbance		
Skin sensitive to light as evidenced by burning easily	Gastric distress as evidenced by doubling over	.68**
Gastric Disturbances		
Vomiting throughout the day	Rash consisting of red discolored patches	.62**
Vomiting throughout the day	Difficult to stay awake especially during the day	.68**
Dermatological Disturbance		
Rash consisting of red discolored patches	Unsteady wide based gait	.68**
Affective Disturbance		
Some mood changes; no interference with activities	Rash consisting of red discolored patches	.68**
Mood changes; interference with some activities	Rash consisting of red discolored patches	.68**
Cognitive Disturbance		
Decline in attention or concentration but doesn't interfere	Rash consisting of red discolored patches	.68**
Gait Disturbances		
Unsteady wide based gait	Mood changes interference with some activities	1.0**

(table continued)

(table continued)

Unsteady wide-based gait	Decline in attention or Concentration but doesn't interfere	1.0*
Sedation		
Difficult to stay awake especially during the day	Some mood change; no interference with activities	1.0*
Difficult to stay awake especially during the day	Frequent tremor	.68**
Control Group		
Sedation		
Difficult to stay awake especially during the day	Skin sensitive to light	.54*
Affective Disturbance		
Mood changes inferences with some activities	Marked impairment of activities significant confusion	.68**

** $p < .01$

* $p < .05$

GENERAL DISCUSSION

The purpose of the present study was two-fold. In Study One, the psychometric properties of the SEIZES-B were investigated. This was achieved by evaluating the interrater reliability of direct observations using the PDC Nursing Assessment Form. Direct observations were completed by two informants, a registered nurse and licensed epileptologist. This comparison was examined to determine if the nurse and epileptologist's ratings were consistent. Then, the convergent validity of the SEIZES-B was examined. The SEIZES-B was compared to direct observations of individuals at the PDC neurology clinic using the Nursing Assessment Form. In Study Two, differences in the baseline level of SE profiles were evaluated in three groups with individuals with ID. These three groups were comprised of individuals with epilepsy taking AEDs, individuals with a diagnosis of epilepsy not taking AEDs, and individuals without epilepsy taking antipsychotic medications.

Assessing the interrater reliability of the direct observation was first examined. This step was chosen to demonstrate the consistency and dependability of the instrument (Mitchell, 1979). Overall, the level of agreement for the majority of the items reflected low positive correlations. They ranged from poor for Intermittent Tremor ($\kappa = -0.06$), to fair for Alert/Awake ($\kappa = 0.53$) at the $p<.05$ level. For the remaining items, all other correlations were considered poor.

Although the direct observational data did not reveal statistical significance, the Nursing Assessment Form has clinical utility because any symptom endorsement (e.g., tremor, sedation) alerts the PDC medical staff that monitoring symptoms in an individual may be necessary and that medication changes may be appropriate. While it was expected that interrater reliability would be high between the nurse and epileptologist, given their level of education and experience, it is unclear why concordance rates were not higher.

However, before the study began, there was initial resistance from the epileptologist to complete direct observation ratings. The epileptologist posited time as a factor. In the research literature, it has been recognized that physicians often lack the time or motivation to accurately complete rating forms (e.g., symptom checklist, surveys, and questionnaires) (Chappell & Smithson, 1997). For example, Traynor and his colleagues (1993) found that researchers' request for physicians to assist in completing surveys was considered an additional demand placed on their already busy lives. In addition, Thom, Lee, Dhillon, Dunne, and Plant (2000) found that physicians sited lack of interest in epilepsy as reasons for declining to participate in research. Perhaps the lack of concordance between the two observers occurred because of differences in temperament or differences among interpretations of items on the Nursing Assessment Form.

The second goal of Study One was to examine the convergent validity of the SEIZES-B by comparing the SEIZES-B to direct observations using the Nursing Assessment Form. An extensive review of the literature revealed a lack of standardized measures of assessing SE in the institutionalized ID population. However, interrater reliability (r = .72) and test-retest reliability (r = .63) using direct care staff as informants demonstrated moderately high reliability coefficients. According to Campbell and Fiske (1959), both reliability and validity concepts require that agreement between measures be demonstrated. Thus, it was essential that the comparison measure for the SEIZES-B items was based on observable data and was verified with interrater reliability. This comparison provided an estimate of convergent validity to show that the instrument accurately measured SE of AEDs. It was hypothesized that the SEIZES-B would have good convergent validity with the epileptologist's ratings from the Nursing Assessment Form because both instruments purported to measure similar constructs, and was designed specifically for individuals with ID and epilepsy.

The results revealed a statistically significant high positive correlation between the SEIZES-B and direct observation for Gait Disturbance, $r = .97$, $p<.001$. According to Cicchetti (1994), .97 is classified as an excellent level of clinical significance. In addition, a statistically low positive correlation was found for Sedation, $r = .26$, $p<.05$. However, the range of reliability coefficients for the remaining items was -.02 to .21. Furthermore, a floor effect observed for the following domains: Respiratory Disturbance, Hair Changes, Tremor, and Drug-Related Dizziness.

Several possible reasons why concordance was poor across the two instruments are offered. First, education level and training between direct-care staff in residential facilities may differ significantly. As a result, some individuals may lack training to delineate possible symptoms of drug SE from comorbid medical conditions (e.g., cerebral palsy, movement disorders, etc.). It is also possible that direct care staff lack understanding of the specific construct being measured despite efforts of scale developers to eliminate unclear questions (Cronbach & Meehl, 1955; DeVellis, 1991). However, given the importance of this topic, education and training direct care staff to detect SE symptoms may be warranted and may help them to detect SE symptoms.

The lack of convergence between direct care staff and the direct observation question the appropriateness of the SEIZES-B when direct care staff is used as raters. According to Mitchell (1979), although indirect measures can yield valuable information, they are usually not as reliable as direct observation measures.

Another possible reason for the low convergence may be related to different administration times of the two instruments. Although the SEIZES-B was administered one-to-two weeks after participants attended neurology clinic to prevent confounding effects of time,

certain behaviors (e.g., vomiting shortly after medication is given) may have occurred in one setting (e.g., home) and not the other (e.g., neurology clinic). Due to shift changes and designated appointments times at clinic, direct care staff and medical staff may not witness a phenomenon and would be subsequently unable to endorse an item on either instrument.

Despite the overall lack of convergence of the SEIZES-B and direct observation, gait disturbance and sedation are consistently identified in the literature as common SE of AEDs (Harbord, 2000; Kustra et al., 2005; Stefan & Feuerstein, in press). While the interrater reliability for Gait Disturbance on the Nursing Assessment Form was $r = .33$, high convergence of this subscale on the SEIZES-B suggests its usefulness in identifying possible SE in combination with direct observations.

The second objective of the present study was to examine group differences of SE profiles in three groups. In Study Two, 15 participants were compared across three groups (AED, non-AED use, and control) on SE profiles of the SEIZES-B. Group membership was the independent variable and SEIZES-B total scores served as the dependent variable. A total of 45 participants were included in this study. A chi-square analysis and ANOVA revealed that the groups did not differ significantly on the variables of age, gender, level of ID, seizure type, and medication type.

A one-way ANOVA revealed a statistically significant difference on the Hair Changes subscale. However, no other statistical differences were found. A floor effect was observed for the non-AED group and control group on the following subscales: Respiratory Disturbance, Hair Changes, Tremor, and Drug-Related Dizziness. Games-Howell post hoc analysis was conducted for Hair Changes. This statistic was chosen because the homogeneity of variance assumption had been violated (Hinkle, Wiersma, & Jurs, 1998). However, no significant difference was detected

between the AED group and control group (p = .18). In the medical literature, hirsutism has been observed as a SE of phenytoin use (Buchanan, 1992; Pellock, 2002). Additionally, alopecia has been observed as a SE of valproic acid use (Buchanan, 1992; Gates, 2000). Despite the fact that the data did not reveal statistically significant differences, the endorsement of one SE symptom may provide useful in making recommendations for titration, alternative drug usage, or discontinuance.

In Study Two, since the sample consisted of a small number of participants in each group and a floor effect was observed, a power analysis was conducted to determine whether possible non-significance findings may have contributed to low power. It was determined a sample of 158 participants would be optimal to achieve a power of .80, using a medium effect size (.05). Although a much larger sample size would have been ideal, it was impossible to attain due to exclusionary criteria and matching practices utilized in this study. Regardless, a larger sample may have lead to the detection of more significant differences across the groups.

Lastly, a series of individual item correlations were examined in order to examine if there was a relationship between certain SE symptoms across the three groups. Based on the analyses, all three groups showed low to very high positive correlations among certain items. Because the ten subscales of the SEIZES-B contained heterogeneous symptoms, low-to-high correlations were not expected. Several subscales, (e.g., Gastric Disturbance, Gait Disturbance, and Sedation) showed perfect positive correlations with other constructs. The relationship between these various constructs warrants a more thorough investigation of these symptoms before making any meaningful interpretation of the endorsed symptom.

The results of the current study extended research on SE of AEDs in the institutionalized ID population. This study represents the first to examine the convergent validity of the SEIZES-

B and interrater reliability of direct observations. While the individual interrater reliability coefficient for Gait Disturbance on the SEIZES-B is considered high by research and clinical standards (Cicchetti, 1994; Mitchell, 1979), the convergent validity of the SEIZES-B and direct observation were poor. Although it is disappointing that the current study did not establish overall high reliability or convergent validity, the psychometric properties of the two instruments provided information that was previously unavailable.

Even though no statistical differences were detected across groups on SE profiles, subtle differences in symptomatology are still a major issue in seizure management. As stated earlier, in individuals with ID, assessments and monitoring of SE are based on informant-based rating scales, changes in observable behaviors, and laboratory monitoring. Based on the results of this study, it is clear that informant-based ratings scales and direct observation alone cannot replace current assessment and management practices.

Continued efforts are being made to improve the pharmacological properties of available AEDs by developing newer AEDs with fewer interactions and untoward SE (Brodie, 1995). For example, pregabalin is a novel AED used for neuropathic pain, as an adjunct therapy for partial seizures, and in generalized anxiety disorder (Hamandi & Sander, 2006). It was designed as a more potent successor to gabapentin (Sills, 2006), and received U.S. Food and Drug Administration approval for use in treating epilepsy, diabetic neuropathy pain and post-herpetic neuralgia pain in June 2005 (Hamandi & Sander, 2006). In Study One, 13 (17.8%) participants were taking pregabalin at the time of chart review. Stefan and Feurstein (in press) found that the most frequent side effects of pregabalin in controlled studies were dizziness, somnolence, ataxia, and weight gain. To date, no research has been conducted to assess the SE of pregabalin in the institutionalized ID population. Future research in this area is warranted.

Similar to that of pharmacological interventions for individuals with epilepsy, treatment of individuals with psychopathology (e.g., bipolar disorder) usually includes a drug regimen. According to Matson, González, Smith, Terlonge, Thorson, and Dixon (2006), who conducted a 20-year review of the literature, SE of pharmacotherapy treatment often include parkinsonism, tardive dyskinesia, akathesia, dystonia, and tremor. Elsewhere in the literature, it has been well documented that antipsychotic medications are not free from untoward SE in the institutionalized ID population (Lipman, 1970). Therefore, it is unlikely that all of the participants in the control group were free from experiencing untoward SE. An explanation for the floor effect observed in the non-AED group and control group could be that direct care staff could not consistently identify or recall when symptoms occurred. However, the lack of identified symptoms may have been compromised by true or random error (Murphy & Davidshofer, 2001).

In the field of ID, treatment of epilepsy and identification and monitoring of SE has been proven difficult. Potential differences in observers, direct care staff, limitations of participant self-report, and methodological constraints, contribute to the complexity of assessment, monitoring, and research investigating drug SE in institutionalized ID populations (Matson, Bielecki, Mayville, & Matson, 2003). Nevertheless, it behooves us to continue focusing on adults with ID and epilepsy and to study, develop, and improve assessment and monitoring techniques of SE. Our ability to improve the psychometrics of SE instruments may improve the quality of life in individuals with ID.

REFERENCES

Adams, R. D., Victor, M. & Ropper, A. H. (1997). *In principles of neurology,* (6th ed.). New York: McGraw-Hill.

Aicardi, J. & Gomes, A. L., (1988). The Lennox-Gastaut syndrome: clinical and electroencephalographic features. In: E. Niedermeyer & R. Degen (Eds.), *Neurology and Neurobiology* (pp. 25-46). Alan R. Liss: New York.

Alexander, D. (1998). Prevention of mental retardation: four decades of research. *Mental Retardation and Developmental Disabilities Research Reviews, 4,* 50-58.

Alvarez, N. (1989). Discontinuance of antiepileptic medications in patients with developmental disability and diagnosis of epilepsy. *American Journal of Mental Retardation, 93*(6), 593-599.

Alvarez, N., Besag, F., & Iivanainen, M. (1998). Use of antiepileptic drugs in the treatment of epilepsy in people with intellectual disability. *Journal of Intellectual Disability Research, 42*(1), 1-15.

Amano, K., Takamatsu, J., Ogata, A., Miyazaki, C., Kaneyama, H., Katsuragi, S., et al. (2000). Characteristics of epilepsy in severely mentally retarded individuals. *Psychiatry & Clinical Neuroscience, 54*(1), 17-22.

American Association of Mental Retardation (1992). *Mental retardation: definition, classification, and systems of support.* Washington, DC: Author.

American Psychiatric Association, (2000). *Diagnostic and statistical manual of mental disorders-text revision,* (4th ed.). Washington, D.C.: Author.

Andriola, M. R., & Vitale, S. A. (2001). Vagus nerve stimulation in the developmentally disabled. *Epilepsy & Behavior, 2*(2), 129-134.

Baroff, G. S. (1991). *Developmental disabilities: psychological aspects.* Austin, TX: Pro-Ed.

Baumeister, A. A., & Sevin, J. A. (1990). Pharmacologic control of aberrant behavior in the mentally retarded: toward a more ration approach. *Neuroscience & Biobehavioral Reviews, 14,* 253-262.

Beirne-Smith, M., Patton, J. R., & Ittenbach, R. (1994). Historical Perspectives (4th ed.). *Mental retardation* (pp. 26-53). New York: Macmillan College Publishing Company.

Bennet, H. S., Dunlop, T., & Ziring, P. R. (1983). Reduction of polypharmacy for epilepsy in an institution for the retarded. *Developmental Medicine and Child Neurology, 25,* 735–737.

Berg, A. T., Shinnar, S., Levy, S. R., Testa, F. M., Smith-Rapaport, S., Beckerman, B., et al. (2001). Defining early seizure outcomes in pediatric epilepsy: the good, the bad and the in-between. *Epilepsy Research, 43*(1), 75-84.

Bernes, S. M., & Kaplan, A. M. (1994). Evolution of neonatal seizures. *Pediatric Clinic of North America, 41*, 1069-1104.

Biasini, F. J., Grupe, L., Huffman, L., & Bray, N. W. (2001). Mental Retardation: A symptom and a syndrome. *Comprehensive textbook of child and adolescent disorders.* New York: Oxford University Press.

Bourgeois, B. (2001). Combination drug therapy (monotherapy versus polytherapy). In: J. M. Pellock, W. E. Dodson & B. Bourgeois (Eds.) *Pediatric epilepsy diagnosis and therapy* (2nd ed.). Demos: New York.

Brodie, M. J. (2001). Do we need any more new antiepileptic drugs? *Epilepsy Research, 45*(1-3), 3-6.

Buchanan, N. (1992). The occurrence, management and outcome of antiepileptic drug side effects in 767 patients. *Seizure, 1*(2), 89-98.

Campbell, D.T., & Fiske, D.W. (1959). Covergent and discriminant validity by the multitriat-multimethod matrix. *Psychological Bulltein, 56,* 81-105.

Carpay, J. A., Alenkamp, A. P., & van Donselaar, C. A. (2005). Complaints associated with the use of antiepileptic drugs: results from a community-based study. *Seizure, 14*(3), 198-206.

Chadwick, D. (1997). Better comparisons of antiepileptic drugs: what measures of efficacy? *Pharmacology World Science, 19*(5), 214-216.

Chappell, B., & Smithson, W. H. (1998). Patient views on primary care services for epilepsy and areas where additional professional knowledge would be welcome**.** *Seizure, 7*(6), 447-457.

Chevrie, J. J., & Aicardi, J. (1978). Convulsive disorder in the first year of life: neurological and mental outcome and mortality. *Epilepsia, 19,* 67-74.

Cicchetti, D. V. (1994). Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. *Psychological Assessment, 6,* 284-290.

Clarke, D. J., Kelley, S., Thinn, K., & Corbett, J. A. (1990). Psychotropic drugs and

mental retardation: disabilities and the prescription of drugs for behaviour and for epilepsy in three residential settings. *Journal of Mental Deficiency Research, 34*, 385-395.

Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences*, 2nd ed. Hillsdale, NJ: Erlbaum.

Cole, A. J. (2002). Evaluation and treatment of epilepsy in multiply handicapped individuals. *Epilepsy & Behavior, 3*(6) (Suppl.1), 2-6.

Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes (1989). *Epilepsia, 30,* 389-399.

Corbett, J. A., Harris, R., & Robinson, R. G. (1975). Epilepsy. In: J. Wortis (Ed.), *Mental retardation and developmental disabilities* (pp. 79-111). New York: Raven Press.

Coulter, D. L. (1993). Epilepsy and mental retardation: An overview. *American Journal on Mental Retardation, 98*(11), 1-10.

Cramer, J. A., & Mattson, R. H. (1993). Quantitative approaches to seizure severity. In H., Meinardi, J. A. Cramer, G. A. Baker, & A. Martins da Silva (Eds.). *Quantitative assessment in epilepsy care* (pp. 55-71). New York: Plenum.

Crocker, A. C. (1992). Data collection for the evaluation of mental retardation prevention activities: the fatal forty-three. *Mental Retardation, 30,* 303-317.

Cronbach, L. J., & Meehl, P.E. (1955). Construct validity in psychological tests. *Psychological* Bulletin, 52, 281-302.

Cuthill, F. M., & Espie, C. A. (2005) Sensitivity and specificity of procedures for the differential diagnosis of epileptic and non-epileptic seizures: a systematic review. *Seizure, 14*(5), 293-303.

DeToledo, J. C., Lowe, M. R., & Haddad, H. (2002). Behaviors mimicking seizures in institutionalized individuals with multiple disabilities and epilepsy: a video-eeg study. *Epilepsy & Behavior, 3*(3), 242-244.

DeVellis, R. F. (1991). Guidelines in scale development. In, *Scale Development: Theory and Applications* (pp. 51-90). Sage Publications: Newbury Park, CA.

Doll, E. A. (1953). *The measurement of social competence: A manual for the vineland social maturity scale.* Washington, DC: Educational Test Bureau.

Drane, D. L. & Meador, K. J. (2002). Cognitive and behavioral effects of antiepileptic drugs. *Epilepsy & Behavior, 3*(5), 49-53.

Drislane, F W., & Schomer, D. L. (1994). Clinical implications of generalized electrographic status epilepticus. *Epilepsy Research, 19*(2), 111-121.

Dykens, E. M., Hodapp, R. M., & Finucane, B. M. (2000). *Genetics and mental retardation syndromes*. Baltimore: Paul H. Brookes Publishing Company.

Ettinger, A. B., Barr, W. B., & Solomon, S. P. (2001). Psychotropic properties of antiepileptic drugs in patients with developmental disabilities. In: O. Devinsky & L. E. Westbrook (Eds.). *Epilepsy and developmental disabilities* (pp. 219–230). Boston: Butterworth-Heinemann.

Eysenck, H. J. (1962). *Know Your I.Q.*. Maryland: Pelican Books.

Faul, F., & Erdfelder, E. (1992). GPOWER: A priori, post-hoc, and compromise power analyses for MS-DOS [Computer software]. Bonn, FRG: Bonn University, Department of Psychology.

Forsgren, L., Edvinsson, S., Blomquist, H. K., Heijbel J., & Sidenvall, R. (1990). Epilepsy in a population of mentally retarded children and adults. *Epilepsy Research, 6*(3), 234-248.

Friis, M. L. (1998). Valproate in the treatment of epilepsy in people with intellectual disability. *Journal of Intellectual Disability Research, 42*(1), 32-35.

Gareri, P., Gravina, T., Ferreri G., & De Sarro, G. (1999). Treatment of epilepsy in the elderly. *Progress in Neurobiology, 58*(5), 389-407.

Gastaut, H. (1970). Clinical and electroencephalographic classification of epileptic seizures. *Epilepsia, 11*, 102-113.

Gastaut, H. (1973). *Dictionary of Epilepsy.* Part 1: definitions. World Health Organization, Geneva: Author.

Gates, J. R. (2000). Side effect profiles and behavioral consequences of antiepileptic medications. *Epilepsy & Behavior, 1*(3), *153-159.*

Gates, J. R., Huf, R. L., & Frost, M. (2001). Vagus nerve stimulation for patients in residential treatment facilities. *Epilepsy and Behavior, 2*, 563-567.

Genton, P. (2000). When antiepileptic drugs aggravate epilepsy. *Brain and Development, 22*(2), 75-80.

Glauser, T. A. (2004). Effects of antiepileptic medications on psychiatric and behavioral comorbidities in children and adolescents with epilepsy. *Epilepsy & Behavior, 5*(3), 25-32.

Goeckner, B. J., Rosenfeld, W. E., & Weber, S. L. (1995). Evaluation of seizure control after phenobarbital withdrawal in a mentally retarded/developmentally disabled population. *Journal of Epilepsy, 8*(2), 93-98.

Goulden, K. J., Shinnar, S., Koller, H., Katz, M., & Richardson, S. A. (1991). Epilepsy in children with mental retardation: a cohort study. *Epilepsia, 32,* 690–697

Greenspan, S., Switzsky, H. N., & Granfield, J. M. (1996). Everyday intelligence and adaptive behavior: a theoretical framework. *Manual of diagnosis and professional practice in mental retardation* (pp. 127-135). Washington, DC: American Psychological Association.

Hamandi, K., & Sander, J. W. (2006). Pregabalin: A new antiepileptic drug for refractory. *Seizure, 15*(2), 73-78.

Harbord, M. G. (2000). Significant anticonvulsant side-effects in children and adolescents. *Journal of Clinical Neuroscience, 7*(3), 213-216.

Harden, C. L. (1997). New antiepileptic drugs. *Medical Update for Psychiatrists, 2*(5), 116-120.

Harris, J. C. (1995). Mental Retardation. *Developmental neuropsychiatry* (pp. 91-126). New York: Oxford University Press.

Hauser, W. A., & Hesdorffer, D.C. (1990). *Epilepsy: frequency, cause and consequences.* New York: Demos.

Heller, J. H. (1969). Human chromosome abnormalities as related to physical and mental dysfunction. *Journal of Heredity, 60*, 239-248.

Herranz, L., Armijo, J. A., & Arteaga, R. (1988). Clinical side effects of phenobarbital, primidone, phenytoin, carbamazepine, and valproate during monotherapy in children. *Epilepsia, 29,* 794–804.

Hinkle, D.E., Wiersma, W., & Jurs, S.G. (1998). *Applied statistics for the behavioral sciences.* New York: Houghton Mifflin Company.

Holmes, G. L. (1997). Classification of seizures and the epilepsies. In S. C. Schachter & D. L. Schomer (Eds.), *The comprehensive evaluation and treatment of Epilepsy: A practical guide* (pp. 1-36). San Diego, CA: Academic Press.

Huf, R. L., Mamelak A., & Kneedy-Cayem, K. (2005). Vagus nerve stimulation therapy: 2-year prospective open-label study of 40 subjects with refractory epilepsy and low IQ who are living in long-term care facilities. *Epilepsy & Behavior, 6*(3), 417-423.

Ieshima, A., & Takeshita, K. (1988). Chromosome abnormalities and epileptic seizures. *Japanese Journal of Human Genetics, 33,* 49-60.

Iivanainen, M. (1998). Phenytoin: effective but insidious treatment for epilepsy with intellectual disability. *Journal of Intellectual Disabilities Research, 42*(1), 24-31.

Jackson, H. (1890). On convulsive seizures. *British Medical Journal, 1,* 703-753.

Janszky, J., Schulz, R., & Ebner, A. (2004). Simple partial seizures (isolated auras) in medial temporal lobe epilepsy. *Seizure, 13*(4), 247-249.

Kane, K., Lee, J., Bryant-Comstock, L., & Gilliam, R. (1996). Assessing the psychometric characteristics of the side effects and life satisfaction inventory (seals) in epilepsy: future validation from lamotrigine clinical trials. *Epilepsia, 37*(Suppl. 5), 4-4.

Kanner, A. M. (2002). Psychiatric comorbidity in patients with developmental disorders and epilepsy: a practical approach to its diagnosis and treatment. *Epilepsy & Behavior, 3,* 7-13.

Kelly, K., Stephen, L. J., & Brodie, M. J. (2004). Pharmacological outcomes in people with mental retardation and epilepsy. *Epilepsy & Behavior, 5*(1), 67-71.

Kerr, M. P. (2002). Behavioral assessment in the mentally retarded and developmentally disabled patients with epilepsy. *Epilepsy & Behavior, 3,* 14-17.

Ketter, T. A., Post, R. M., & Theodore, W. H. (1999). Positive and negative psychotropic effects of antiepileptic drugs in patients with seizure disorders. *Neurology, 53*(1), 52–66.

Koo, T. S. & Holmes, G. L. (1999). Eeg and clinical predictors of medically intractable childhood epilepsy. *Clinical Neurophysiology, 110,* 1245-1251.

Kotagal, P., Rothner, A. D., Erenberg, G., Cruse, R. P., & Wyllie, E. (1987). Complex partial seizures of child onset: a five-year follow-up study. *Archives of Neurology, 44,* 1177-1180.

Kumada, T., Ito, M., Miyajima, T., Fujii, T., Okuno, T., Go, T., et al. (2005). Multi-institutional study on the correlation between chromosomal abnormalities and epilepsy. *Brain and Development, 27*(2), 127-134.

Kustra, R. P., Meador, K. J., Evans, B. K., Leschek-Gelman, L. M., Groenke, D. A., Hammer, A. E., et al., (2005). Lamotrigine therapy in patients requiring a change in antiepileptic drug regimen. *Seizure, 14*(4), 254-261.

Lennox, W. G. (1960). *Epilepsy and Related Disorders.* Boston: Little, Brown, and Company.

Lipman, R. S. (1970). The use of psychopharmacological agents in residential facilities for the retarded. In F. Menolascino (Eds.), *Psychiatric approaches to mental retardation*. New York: Basic Books, p. 387-398.

Lombroso, C. T. (1983). Prognosis in neonatal seizures. In: A. V. Delgado-Escueta, C. G. Wasterlain , D.M. Treiman, & R.J. Porter, (Eds.). *Advances in neurology: status epilepticus* (pp. 101-113). New York: Raven Press.

MacMillan, D. L., Gresham, F. M., & Siperstein, G. N. (1995). Heightened concerns over the 1992 AAMR definition: advocacy versus precision. *American Journal of Mental Retardation, 100*(1), 87-97.

Mangano, S., Fontana, A., & Cusumano, L. (2005). Benign myoclonic epilepsy in infancy: neuropsychological and behavioural outcome. *Brain and Development, 27*(3), 218-223.

Marcus, J. C. (1993). Control of epilepsy in mentally retarded population: lack of correlation with iq, neurological status, and electroencephalogram. *American Journal on Mental Retardation, 98,* 47-51.

Mariani, E., Gerini-Strambi, L., Sala. M., Erminio., C., & Smirne, S. (1993). Epilepsy in institutionalized patients with encephalopathy: clinical aspects and nosological considerations. *American Journal on Mental Retardation, 98,* 27-33.

Matson, J. L., Bamburg, J. W., Mayville, E. A., Pinkston, J., Bielecki, J., Kuhn, D., et al. (2000). Psychopharmacology and mental retardation: a 10 year review (1990–1999). *Research in Developmental Disabilities, 21*(4), 263-296.

Matson, J. L., Bielecki, J., Mayville, S. B., & Matson, M. L. (2003). Psychopharmacology research for individuals with mental retardation: methodological issues and suggestions. *Research in Developmental Disabilities, 24*(3), 149-157.

Matson, J. L., González, M. L., Smith, K. R., Terlonge, C., Thorson, R. T., & Dixon, D. R. (2006). Assessing side effects of pharmacotherapy treatment of bipolar disorder: A 20-year review of the literature. *Research in Developmental Disabilities, 27,* 467-500.

Matson, J, L., Laud, R. B., González, M. L., Malone, C. J., & Swender, S. L. (2005). The reliability of the Scale for the Evaluation and Identification of Seizures, Epilepsy, and Anticonvulsant Side Effects-B (SEIZES B). *Research in Developmental Disabilities, 26*(6), 593-599.

Matson, J. L., Luke, M. A., & Mayville, S. B. (2004). The effects of antiepileptic medications on the social skills of individuals with mental retardation. *Research in Developmental Disabilities, 25, 219-228.*

Matson, J. L., Mayville, E. A., & Bamburg, J. W. (2001). An analysis of side-effect profiles of anti-seizure medications in persons with intellectual disabilities using the Matson

Evaluation of Drug Side Effects (MEDS). *Journal of Intellectual & Developmental Disability, 26*(4), 283-295.

Matson, J. L., & Baglio, C. S. (1998). *Administrator's Manual: Matson Evaluation of Drug Side Effects (MEDS).* Baton Rouge, LA: Disability Consultants, LLC.

Mattson, R. H. (1996). The role of the old and the new antiepileptic drugs in special populations: mental and multiple handicaps. *Epilepsia, 37*, 45-53.

Mayville, E. A., & Matson, J. L. (2004). Assessment of seizures and related symptomatology in persons with mental retardation. *Behavior Modification, 28*(5), 679-693.

Meldrum, B. (2002). Do preclinical seizure models pre-select certain adverse effects of antiepileptic drugs. *Epilepsy Research, 50*(1-2), 33-40.

McDermott, S., Moran, R., & Platt, T. (2005). Prevalence of epilepsy in adults with mental retardation and related disabilities in primary care. *American Journal on Mental Retardation, 110*(1), 48-56.

McDonnell, G. V., & Morrow, J. I. (1996). An audit of the new antiepileptic drugs in clinical neurological practice. *Seizure, 5*(2), 127-130.

McKee, J. R., Sunder, T. R., Fine-Smith, F., Vuong, A., Varner, J.A., Hammer A.E., et al. (2003). Lamotrigine as adjunctive therapy in patients with refractory epilepsy and mental retardation. *Epilepsy & Behavior, 4*(4), 386-394.

McLaren, J., & Bryson, S. E. (1987). Review of recent epidemiological studies in mental retardation: prevalence, associated disorders, and etiology. *American Journal of Mental Retardation, 92,* 243-254.

Mitchell, S. K. (1979). Interobserver agreement, reliability, and generalizability of data collected in observational studies. *Psychological Bulletin, 86,* 376-390.

Mohanraj, R., & Brodie, M. J. (2005). Pharmacological outcomes in newly diagnosed epilepsy**.** *Epilepsy & Behavior, 6*(3), 382-387.

Murphy, K., & Davidshofer, C. (2001). The Consistency of Test Scores. *In Psychological Testing (5th Ed.*), (pp. 108-124). Prentice Hall: Upper Saddle River, NJ.

Okumura, A., Watanabe, K., Negoro, T., Ishiguro, Y., Miura, K., Matsumoto, A., et al. (2000). MRI findings in patients with symptomatic localization-related epilepsies beginning in infancy and early childhood. *Seizure, 9*(8), 566-571.

Pary, R. (1993). Mental retardation, mental illness, and seizure diagnosis. *American Journal on Mental Retardation, 98,* 58-62.

Patil, K. M., & Bodhankar, S. L. (2005). Simultaneous determination of lamotrigine, phenobarbitone, carbamazepine and phenytoin in human serum by high-performance liquid chromatography. *Journal of Pharmaceutical and Biomedical Analysis, 39,* 181-186.

Patsalos, P. N., & Perucca, E. (2003). Clinically important drug interactions in epilepsy: interactions between antiepileptic drugs and other drugs. *The Lancet Neurology, 2*(8), 473-481.

Patton, J. R., & Jones, E. (1994). Definitional Perspectives (4th ed.). *Mental retardation* (pp. 26-53). New York: MacMillan College Publishing Company.

Perucca, E. (2002). Patient-tailored antiepileptic drug therapy: predicting response to antiepileptic drugs. *International Congress Series, 1244,* 93-103.

Perucca, E., Beghi, E., Dulac, O., Shorvon, S., & Tomson, T. (2000). Assessing risk to benefit ratio in antiepileptic drug therapy. *Epilepsy Research, 41*(2), 107-139.

Pellock, J. M. (2002). Treatment considerations: traditional antiepileptic drugs. *Epilepsy & Behavior, 3*(6), 18-23.

Pellock, J. M. & Hunt, P. A. (1996). A decade of modern epilepsy therapy in institutionalized mentally retarded patients. *Epilepsy Research, 25*(3), 263-268.

Pellock, J. M., & Morton, L. D. (2000). Treatment of epilepsy in the multiply handicapped. *Mental Retardation and Developmental Disabilities Research and Review, 6***,** 309–323.

Poindexter, A. R., Berglund, J. A., & Kolstoe, P. D. (1993). Changes in antiepileptic drug prescribing patterns in large institutions: preliminary results of a five-year experience. *American Journal on Mental Retardation,* 98, 34-40.

Porter, R. J., & Meldrum, B. S. (1990). Antiepileptic drugs (7^{th} Ed). In: B.G. Katzung (Ed.), *Basic and clinical pharmacology* (pp. 386-408). Connecticut: Appleton & Lange.

Rantakallio, P., von Wendt, L., & Koivu, M. (1987). Prognosis of perinatal brain damage: a prospective study of a one year birth cohort of 12 000 children. *Early Human Development, 15*(2), 75-84.

Reijs, R., Aldenkamp A. P., & De Krom, M. (2004). Mood effects of antiepileptic drugs. *Epilepsy & Behavior, 5*(1), 66-76.

Richardsson, S. A., Koller, H., & Katz, M. (1981). A functional classification of seizures and its distribution in a mentally retarded population. *American Journal of Mental Deficiency, 85,* 457-466.

Rogvi-Hansen, B., & Gram, L. (1995). Adverse effects of established and new antiepileptic drugs: an attempted comparison. *Pharmacology & Therapeutics, 68(*3), 425-434.

Rutecki, P. A., & Gidal, B. E. (2002). Antiepileptic drug treatment in the developmentally disabled: treatment considerations with the newer antiepileptic drugs. *Epilepsy & Behavior, 3,* 24-31.

Scheerenberger, R. C. (1983). *A history of mental retardation*. Baltimore: Brookes Publishing Company.

Schiff, N. D., Labar, D. R., & Victor, J. D. (1999). Common dynamics in temporal lobe seizures and absence seizures. *Neuroscience, 91*(2), 417-428.

Sills, G. J. (2006). The mechanisms of action of gabapentin and pregabalin**.** *Current Opinion in Pharmacology, 6*(1), 108-113.

Singh, B. K., & Towle, P. O. (1993). Antiepileptic drug status in adult outpatients with mental retardation. *American Journal on Mental Retardation, 98,* 41-46.

Sparrow, S. S., Balla, D. A., & Cicchetti, D. V. (1984). *Vineland adaptive behavior scale: Expanded form manual.* Minnesota: Circle Press: American Guidance Services.

Specht, U., Elsner, H., May, T. W., Schimichowski, B., & Thorbecke, R. (2003). Postictal serum levels of antiepileptic drugs for detection of noncompliance. *Epilepsy & Behavior, 4*(5), 487-495.

Stefan, H. & Feurstein, T. J. (In press). Novel anticonvulsant drugs. Pharmacology & Therapeutics.

Steffenburg, U., Hagberg, G., & Kyllerman, M. (1996). Characteristics of seizures in a population-based series of mentally retarded children with active epilepsy. *Epilepsia, 37,* 850-856.

Stein, R. A., & Strickland, T. L. (1998). A review of neuropsychological effects of commonly used prescription medications. *Archives of Clinical Neurology, 13,* 259-284.

Sundaram, M., Sadler, R. M., Young G. B., & Pillay, N. (1999). EEG in epilepsy: current perspectives. *Canadian Journal of Neurological Science, 26,* 255–262.

Tabachnick, B. G., & Fidell, L. S. (1996). *Using multivariate statistics* (4th ed.). Needham Heights: Allyn & Bacon.

Thom, G. A., Lee, H. S., Dhillon, R., Dunne, J. W., & Plant, A. J. (2000). The general practice management of epilepsy in perth, western australia. *Journal of Clinical Neuroscience, 9*(1), 30-32.

Traynor, V., Neary, S., Bridges-Webb, C., Miles, D. A., Britt, H., & Charles, J. (1993). Recruiting general practitioners for survey research. *Australian Family Physician, 22*(5), 794-795.

Trimble, M. R., Ring, H. A., & Schmitz, B. (2000). Epilepsy. In B. S. Fogel, R. B. Schiffer, & S. M. Rao (Eds.), *Synopsis of neuropsychiatry* (pp. 469-489). Philadelphia: Lippincott, Williams, & Wilkins.

Tuxhorn, I. E. B. (2005). Somatosensory auras in focal epilepsy: a clinical, video eeg and mri study. *Seizure, 14*(4), 262-268.

Vining, E. P. G., Carpenter, R. O., & Aman, M. G. (1999). Antiepileptics (anticonvulsants). In J. S. Werry & M. G. Aman (Eds.), *Practitioner's guide to psychoactive drugs for children and adolescents 2nd ed.* (pp. 355-385). New York: Plenum Publishing Corporation.

Waisburg, H., & Alvarez, N. (1998). Carbamazepine in the treatment of epilepsy in people with intellectual disability. *Journal of Intellectual Disability Research, 42,* 36-40.

Wilfong, A. A. (2002). Treatment considerations: role of vagus nerve stimulator. *Epilepsy & Behavior, 3,* 41-44.

Wyllie, E. (1993). *The treatment of epilepsy: Principles and practice***.** Philadelphia: Lippincott, Williams & Wilkins.

Yamanouchi, H., Imataka, G., Nakagawa, E., Nitta, A., Suzuki, N., Hirao, J., et al. (2005). An analysis of epilepsy with chromosomal abnormalities. *Brain and Development, 27*(5), 370-377.

Zigler, E., Balla, D., & Hodapp, R. (1984). On the definition and classification of mental retardation. *American Journal of Mental Deficiency, 89,* 215-230.

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